THE TREATMENT OF EXPERIMENTAL TUBERCULOSIS IN GUINEA-PIGS AND RABBITS BY TAURIN, ALONE AND IN COMBINATION WITH GOLD CHLORID AND SODIUM OLEATE *

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Ever since the successful treatment of syphilis by chemotherapy in the hands of Ehrlich and Hata and others, many attempts have been made to affect tuberculosis in a similar manner. Hexheimer, Altmann, and Bernhardt[1] treated lupus with salvarsan with apparently good effect. In 1912 Grafin von Linden,[2] working under the direction of Finckler, tried the efficacy of several copper derivatives in experimental tuberculosis. In her experiments she first employed emulsions of several copper salts, but, finding them strongly irritating, finally utilized an emulsion of copper and lecithin, which not only had no objectionable irritating effects, but seemed to exercise a distinctly curative action on the experimental lesions in guinea-pigs. Similar results were reported by Meissen and Straus,[3] who used the same preparation in the treatment of lupus. Bodmer[4] also reported success in treating a case of human tuberculosis, and Weiss[5] obtained good results in a single case of tuberculosis of the bladder. Koga[6] and Otani[7] have reported favorable results, both in experimental and in clinical tuberculosis, with the use of a preparation of potassium cyanid and copper, to which the name cyanocuprol has been given.

On the other hand, Moewes and Jauer[8] were unsuccessful in treating human beings with copper preparations, and found them equally ineffective experimentally in guinea-pigs. In previous, unreported experiments I found that copper derivatives had little preventive power

* Received for publication January 17, 1917.

1 Jahresb. ü. d. Ergebn. d. Immunitätsf., 1912, 8, p. 13.
2 Beit. z. Klin. d. Tuberk., 1912, 23, p. 201.
3 Ibid., p. 223.
4 München. med. Wchnschr., 1913, 60,[2] p. 1758.
5 Ibid., 1914, 61,[2] p. 1558.
6 Jour. Exper. Med., 1916, 24, pp. 107, 149.
7 Ibid., p. 187.
8 München. med. Wchnschr., 1914, 61,[1·2] p. 1439.

in experimental tuberculosis and no curative value whatsoever. Of 10 guinea-pigs that had been treated with copper emulsion, 7 died within 1 month with characteristic lesions. Corper, DeWitt, and Wells[9] obtained similar negative results with copper compounds.

Among other metals that have been employed in tuberculosis is gold cyanid, tried by Bruck and Gluck[10] and Hauck[11] in lupus with no beneficial effect, but with great danger on account of its toxicity. Mehler and Asher[12] used a substance known as Borcholin or enzytol, which by liberating cholin in the animal body had some apparent effect in surgical tuberculosis. Similar results were obtained with the same preparation by Baisch.[13]

Kahle[14] tried a preparation of silicic acid in guinea-pigs that had been infected with tubercle bacilli, and reports that the lesions became encapsulated and then cicatrized. Noguchi[15] treated tubercle bacilli with sodium oleate and found that such treated microorganisms could be used to produce a certain degree of protection against untreated and virulent cultures of the same strain. Zeuner[16] found the same preparation of value and suggested its use in human cases. Gold and sodium chlorid has been claimed to have some effect on experimental tuberculosis by Gibbs and Shirley.[17]

In further, unreported experiments I employed a colloidal mixture of gold chlorid and sodium oleate in experimental tuberculosis in guinea-pigs. When these two substances thus combined were inoculated before the actual infection took place, there seemed to be a distinct inhibition of the disease in the treated animals. Nothing, however, approaching a curative effect after infection had begun could be demonstrated.

Weichardt[18] found that retardin or antikenotoxin extracted from egg albumin had the property of neutralizing toxins of B. tuberculosis; and under his guidance Fluhler[19] experimented extensively with this substance in experimental tuberculosis in goats. Control animals succumbed to infection, whereas goats that had been previously treated

[9] Jour. Am. Med. Assn., 1913, 60, p. 887.
[10] München. med. Wchnschr., 1913, 60,[2] p. 57.
[11] Ibid., p. 1824.
[12] Ibid., p. 748.
[13] Ibid., 1914, 61,[2] p. 1613.
[14] Ibid., p. 752.
[15] Centralbl. f. Bakteriol., I, O., 1909, 52, p. 85.
[16] Ztschr. d. Tuberk., 1913, 20, p. 389.
[17] Quoted in Schumaker's Treatise on Materia Medica and Therapeutics, 1908.
[18] Centralbl. f. Bakteriol., I, O., 1912, 62, p. 539.
[19] Zentralbl. f. d. ges. Physiol. u. Path. d. Stoffwechs., 1909, 10, p. 564.

with antikenotoxin withstood infection excellently and showed only localized lesions about the point of inoculation. In experiments to which Weichardt has already made reference,[20] I found that retardin worked moderately well as a preventive in experimental tuberculosis in guinea-pigs, but had no curative effect.

Another line of possible therapeutic investigation occurred to me, which I believe has not been sufficiently considered. The liver and the bile have, as is known, certain very definite and striking relations to bacterial infections. Posselt[21] has considered these relations in great detail and drawn the conclusion that the liver in general acts as a filter for bacteria and that the bile has a distinct inhibitive effect on the growth of many microorganisms, tho on bacteria of the colon-typhoid group its action is favorable rather than disadvantageous. Zehden[22] some years ago made a very careful study of the literature in reference to liver tuberculosis and was able to come to rather definite and important conclusions. It is evident that tubercles occur with relative infrequency in the liver, and that when they are found there it is probable that they have arisen during the later stages of the disease; in other words, a resistance which previously existed would seem to have been broken down (Dallemagne[23]). There is further evidence of a distinct tendency of liver tubercles to heal (Sabourin[24]). This action of the liver cells on the tubercle bacillus is referable undoubtedly to the bile. Kotlar[25] endeavored to find tubercle bacilli in broken-down tubercles which opened into the bile ducts, in vain. Létienne[26] was never but once able to find tubercle bacilli microscopically in the bile, and never obtained their growth in cultures. Brissaud and Toupet[27] were not able to find tubercle bacilli in the liver of patients dead of the disease. Hanot and Lauth[28] found the organisms in experimental tuberculosis in very small numbers in the liver. Maffucci and Sirleo[29] found that tubercle bacilli injected through the umbilical cord in embryos or through the portal vein in adults were taken up by the liver cells and destroyed; this action would apparently be due to the presence of the

[20] Cited by Schwenk, Jahresb. ü. d. Ergebn. d. Immunitätsf., 1912, 8, p. 44.
[21] Ergebn. d. allg. Path., 1915, 17, p. 719.
[22] Centralbl. f. allg. Path. u. path. Anat., 1897, 8, p. 468.
[23] Du foie tuberculeux. Thèse d'agrégation, Univ. de Bruxelles., Paris, 1891.
[24] Archives de physiol. norm. et path., 1883, 15, p. 52.
[25] Ztschr. f. Heilk. Prager Vierteljahrsschrift, 1894, 15, p. 121.
[26] Arch. de méd. expér. et d'anat. path., 1891, 3, p. 761.
[27] Études exp. sous la direct. du prof. Verneuil, I, Paris, 1887.
[28] Études exp. sous la direct. du prof. Verneuil, II, Paris, 1888.
[29] Centralbl. f. allg. Path. u. path. Anat., 1895, 6, p. 305.

bile within the cell, according to Zehden.[22] Kühne suggested the use of taurin in a complicated culture medium for the growth of the tubercle bacillus. Meyer[30] found that bovine tubercle bacilli grew well on potato media which contained cattle bile, but not well when mixed with human bile, and that the reverse was also true. Proskauer and Beck,[31] after careful analysis of these synthetic media for tubercle bacilli suggested by Kühne, found that taurin was not only not necessary, but actually inhibited the growth of tubercle bacilli.

These facts, suggesting some relation between constituents of the bile and a resistance to infection with the tubercle bacillus, led us to incorporate the most characteristic aminoacid of the bile, taurin, $NH_2.CH_2.CH_2.SO_2.OH$, in a 'combination' treatment, with which the first part of this report deals. In later experiments taurin alone was used, and apparently the encouraging results obtained in our earlier experiments with the combination were due in large part, if not entirely, to the taurin and not to the gold chlorid and sodium oleate combined with it in the earlier experiments.

The materials employed in this investigation were prepared as follows:

1. A colloidal solution of sodium gold chlorid was made by dissolving the pure salt (Kahlbaum or Merck) in distilled water in the proportion of 5 mg. to 100 c.c., and then adding 1 gm. of sodium oleate. The mixture, which forms a purplish colloidal solution, was then sterilized before use.

2. The taurin employed was kindly prepared for us by Dr. K. Miyake in the Rudolph Spreckels physiological laboratory of the University of California. After making vain attempts to synthesize taurin by Strecker's method,[32] and having found that the amount recoverable from ox bile was very small, Miyake finally found it could be obtained in quantity from the muscle of shell fish, where it is known to be abundant. For this purpose the common abalone of the Pacific coast, Haliotis, proved the best source because of its structure, which is almost entirely muscular. Mendel and Jaffa[33] had already shown that taurin was present in relatively large amounts in the muscle of this animal.

The method finally employed with success and with a relatively large yield of taurin was as follows:

1. Fresh abalone meat is chopped fine in a meat grinder.

2. The ground meat is boiled with a little water in a double boiler for 2 or 3 hours, and the whole boiled contents subjected to pressure to extract the juice.

3. The extracted juice is treated with a saturated aqueous solution of potassium aluminum sulfate, which is added in sufficient quantity to precipitate all the fibrous and albuminous contents. The mixture is allowed to cool and is then filtered through flannel.

[30] Diss. Giessen, 1910. Quoted by Cornet and Kossel, Kolle and Wassermann's Handb. d. pathogen. Mikroorganismen, 1913, 5, p. 481.

[31] Ztschr. f. Hyg. u. Infektionskr., 1894, 18, p. 128.

[32] Jour. Am. Chem. Soc., 1915, 37, p. 2604.

[33] Beit. z. chem. Physiol., 1903-4, 5, p. 582.

4. To the filtrate is added a saturated solution of barium hydroxid until no further precipitate of sulfates is formed. This precipitate is removed by filtration.

5. The excess of barium in the filtrate is precipitated with CO_2 in the form of barium carbonate. The filtrate is then heated and allowed to stand for from 10 to 12 hours to allow the last trace of barium to be precipitated.

6. The mixture is then filtered, neutralized with acetic acid, and evaporated until taurin begins to crystalize out. Two or three recrystallizations will produce taurin in the form of characteristic crystals, and in relatively pure form.

The first three of the following experiments were carried out in a private laboratory under conditions which precluded more complete study, particularly in reference to the histologic aspects of the problem. In the latter experiments, as will be seen, our observations at autopsy were fully checked by microscopic examination. The method of infection with tubercle bacilli has varied somewhat in the evolution of the work and will therefore be described separately under each experiment.

EXPERIMENT 1

Sixteen guinea-pigs approximately 400 gm. in weight were inoculated subcutaneously over the right pectoral muscle, each with $\frac{1}{16}$ of a 6-months-old culture of bovine tubercle bacillus on glycerin potato (kindly furnished me by Professor Weichardt, of Erlangen, Germany). The whole culture had been suspended in 16 c.c. of sterile physiologic salt solution, rubbed up in a mortar, and shaken in a mechanical apparatus for 2 hours until homogeneous. Each dose comprised a volume of 1 c.c. The inoculated animals were then divided into 3 series.

Series 1. On Oct. 19, 1913, 24 days after inoculation, the treatment of 6 animals (3, 5, 16, 18, 19, and 25) was begun and carried out as follows. The treatment lasted for 48 days and on every 2nd or 3rd day a subcutaneous injection either of taurin (dose 0.05 or 0.1 gm.) alone or of a combination of taurin, 50 mg., and of gold chlorid, 0.5 mg., plus sodium oleate, 10 mg., injected successively, was given. In the period of treatment the total amount of taurin alone given in 14 doses was 1.225 gm., and the total amounts of the substances given in combination were—taurin, 250 mg.; sodium oleate, 50 mg., and gold chlorid, 2.5 mg.

Series 2. In 2 animals (11 and 31) treatment was begun 40 days after inoculation. Nine injections only were given.

Series 3. This series, comprising 8 animals (1, 2, 6, 7, 28, 35, 37, and 39), was left untreated as controls.

The results are summarized in Table 1.

TABLE 1

RESULTS OF EXPERIMENT 1

Guinea-Pig	Day of Death	Weight (gm.) −= Loss. +=Gain		Postmortem Examination
		SERIES 3. CONTROLS		
2	2nd	− 20		No distinctive lesions
37	2nd			No distinctive lesions
28	31st	− 40		Lung showed diffuse tuberculous areas. Liver and spleen were enlarged, contained many tubercles. Axillary lymph nodes enlarged and caseated
6	43rd	− 55	Av. loss 21 gm.	Nodules of lung less diffuse than in Guinea-pig 28. Liver, spleen, and lymph nodes similar to those organs in 28
1	45th	− 30		Similar to Guinea-pig 28
7	45th	− 40		Similar to Guinea-pig 28
39	64th	+ 20		Lung full of diffuse tuberculous areas. Liver, spleen, and lymph nodes contained many large tuberculous nodules, which were caseated
35	Killed on 85th	+ 15		Similar to Guinea-pig 39
		SERIES 2 (TREATED OVER A SHORTER PERIOD)		
31	63rd	+ 35	Av. gain 80 gm.	Lung contained good-sized but well-localized tubercles. Liver enlarged; nodules whitish and well localized. Spleen full of many small-sized nodules. Lymph nodes enlarged and caseated
11	Killed on 85th	+125		Few well-localized nodules in lung only
		SERIES 1 (TREATED OVER A LONGER PERIOD)		
3	Killed on 38th	− 25	Av. gain 37 gm.	Small distinct nodules in lung. Nodules in liver and spleen small but definite. Axillary lymph nodes enlarged and caseated
5	45th	+ 60		Similar to Guinea-pig 3
18	52nd	+ 15		Lung contained good-sized but localized nodules. Liver enlarged; nodules whitish and well localized. Spleen full of many small-sized nodules. Lymph nodes enlarged and caseated.
25	Killed on 61st	+ 15		Lung contained white well-localized nodules in small numbers. Liver and spleen enlarged, containing a few tubercles. Lymph nodes enlarged, with a small area of caseation
16	Killed on 85th	+ 90		Surface of the lung for the most part smooth. A few discrete nodules visible on cut surface. Surface of liver cirrhotic. Definite tubercles on surface were rare, and well localized
19	Killed on 85th	+ 70		Lung contained many small nodules on the surface, which were well localized. Liver surface for the most part smooth. Spleen showed puckered discrete nodules of varying size; not caseated. On section, well localized

Among the controls all the animals save one died within 64 days, and 5 of these 7 died of tuberculosis. The average loss of weight in these animals and the one that was killed was over 23 gm. In the treated series No. 1, only 2 animals died in the first 60 days; one was killed during this period; and the other three were killed subsequently to observe any change in the lesions. At the time of death or killing the average gain in weight for this series was over 37 gm., as contrasted with the average loss in the other series. In the treated series No. 3, there were only 2 animals, one of which died and one of which was killed after 85 days; the average gain in these two animals was 80 gm. The postmortem findings in a general way would seem to indicate an arresting of the process, and in some instances an attempt at repair; but microscopic examination would be necessary in detail to determine this point.

EXPERIMENT 2

This experiment was carried out in a manner similar to that of Experiment 1, with the exception that a human strain of tubercle bacillus (obtained from the Cutter laboratory, Berkeley) was employed. Twenty guinea-pigs, weighing on the average 350 gm., were inoculated subcutaneously with $\frac{1}{38}$ of an old culture of B. tuberculosis (humanis) suspended in 1 c.c. of salt solution. The animals were then divided into 4 groups of 5 each, and 1 group was reserved as control without treatment. The outline of treatment for the other three groups follows.

Series 3. Treatment was begun 7 days after inoculation and lasted 3 months; during this period 11 injections of taurin alone in a dose of from 0.1 to 0.15 gm., and 7 injections of taurin plus the combination of gold chlorid, 0.4 mg., and sodium oleate, 10 mg., were given.

Series 2. Treatment was begun 14 days after inoculation and lasted 3 months less a few days; 15 injections of taurin alone were given and 4 injections of a combination of taurin and gold chlorid and sodium oleate in amounts similar to those of Series 3.

Series 1. Treatment was begun 21 days after inoculation, and lasted 10 weeks, during which 14 injections of taurin were given (0.1 to 0.15 gm.), and 4 injections of taurin plus the combination of gold chlorid and sodium oleate, as in the other groups. The results of this experiment are expressed in Table 2.

It would seem evident from this experiment that not only was the process arrested, but, judged from the weights and gross postmortem findings, all the animals in Series 3 and 2 were nearly or entirely cured

TABLE 2

RESULTS OF EXPERIMENT 2

Guinea-Pig	Day of Death	Weight (gm.) — = Loss. + = Gain		Postmortem Examination
		CONTROLS		
150	28th	— 85		Lung, liver, and spleen contained many small tubercles. Lymphatic glands enlarged and caseated
142	61st	+ 45	Av. loss 17 gm.	Lung full of large diffuse tuberculous masses. Liver and spleen enlarged, containing many tubercles. Lymphatic glands enlarged and caseated
141	66th	— 10		Similar to Guinea-pig 142
144	70th	— 45		
148	79th	+ 10		
		SERIES 3 (TREATED EARLIEST AND LONGEST)		
41	Killed on 82nd	+105		Lung showed small whitish well-localized tubercles. Liver and spleen were enlarged, and contained many small but localized nodules. Lymphatic glands enlarged and caseated
57	Accidentally died on 106th	+ 70	Av. gain 137 gm.	Lung, liver, and spleen similar to Guinea-pig 41's. Lymphatic glands enlarged but very slightly caseated
62		+185		Lymph nodes enlarged and hardened, but not caseated. Lung and liver showed no definite tubercles. Spleen still contained definite tubercles
75	Killed on 108th	+205		
64		+120		
		SERIES 2 (TREATED LATER THAN SERIES 1 BUT FOR SAME PERIOD)		
53	67th	+ 10		Lung showed good-sized whitish nodes. Liver and spleen enlarged, but no definite nodules visible. Lymphatic glands enlarged and hardened, but not caseated
42	Killed on 108th	+310	Av. gain 169 gm.	Lung had a few well-localized nodes. Liver enlarged; no definite nodes. Lymphatic glands enlarged
49	Killed on 108th	+ 65		Lung and liver contained a few well-localized whitish tubercles. Spleen—no definite tubercles visible. Lymphatic glands enlarged
52	Killed on 108th	+200		No definite nodes in lung, liver, or spleen
63	Killed on 108th	+266		Similar to Guinea-pig 52
		SERIES 1 (TREATED LAST AND SHORTEST PERIOD)		
143	76th	+ 60		Lung contained whitish well-localized tubercles. Liver was cirrhotic and contained a few tubercles. Lymphatic glands enlarged
135	106th	+ 55		Lung contained cavity with indurated wall. Liver was enlarged and contained a few tubercles. Spleen enlarged, no tubercles. Lymph nodes enlarged
133	Killed on 108th	+ 95	Av. gain 94 gm.	Lung—a few well-circumscribed nodules with small cavity with indurated walls. Liver and spleen were enlarged and contained numerous tubercles. Lymphatic glands enlarged and caseated
140	Killed on 108th	+ 95		Lung—well-circumscribed tubercles and a cavity. Liver and spleen were enlarged and contained a few tubercles. Lymphatic glands enlarged and indurated
145	Killed on 108th	+165		No definite nodules found in lung, liver, or spleen. Lymph nodes enlarged and hardened

of active tuberculosis. Whether or not living tubercle bacilli still remained in the lesions was not determined. The animals in Series 1 apparently were almost as favorably affected as those in the earlier series, tho the lesions, as indicated by cavity-formation, had proceeded further before the treatment was begun.

It would appear, then, that under the conditions mentioned, which were not so exactly determined as would be desirable in point of view of dosage, guinea-pigs were cured by the combined treatment after a subcutaneous inoculation of either bovine or human tubercle bacilli.

EXPERIMENT 3

In this experiment a modification was made of the experiments already described in that the guinea-pigs were inoculated intraperitoneally with a human culture similar to the one employed in Experiment 2 (obtained from the Cutter laboratory). Seventeen guinea-pigs

TABLE 3

RESULTS OF EXPERIMENT 3

Guinea-Pig	Day of Death	Weight (gm.) −=Loss. +=Gain		Postmortem Examination
		CONTROLS		
33	63rd	— 80		Lung, liver, spleen, peritoneum, and omentum, all show many diffuse tubercles. Lymph nodes enlarged and caseated
17	67th	—350	Av. loss 142 gm.	
21	72nd	—145		
18	78th	— 65		Same as Guinea-pig 33
20	78th	—165		
30	78th	— 10		
19	90th	—180		
		TREATED ANIMALS		
24	75th	—180		Lung—many discrete nodules. Liver and spleen enlarged; no definite nodules visible. Peritoneum — no nodules visible. Lymph nodes enlarged, not caseated
34	81st	—125		Similar to Guinea-pig 24, except that inguinal and mesenteric lymph nodes were partly caseated
23		—195	Av. loss 49.5 gm.	Lung—very few tubercles remain. Liver—a few discrete tubercles. No tubercles found in spleen or peritoneum. Lymph nodes enlarged, not caseated
22		+ 20		Similar to Guinea-pig 23
27		—110		Guinea-pigs 27, 29, and 25 similar to Guinea-pig 24, but lymphatic glands showed a few central caseated areas
29	Killed on 90th	—125		
25		+ 35		
26		+ 35		Guinea-pigs 26, 31, and 32 had lesions even less marked than those in the preceding
31		+ 50		
32		+100		

were given intraperitoneal injections of 1 c.c. of a suspension of tubercle bacilli containing from 5 to 17 c.c. Seven of the animals were left as controls without treatment. Fourteen days later injections of taurin were begun subcutaneously in the remaining 10 animals. Sixteen of these injections were given in a dosage of from 0.1 to 0.2 gm. every 3 days and were followed by 8 injections of taurin plus gold chlorid (0.2 mg.) and sodium oleate (10 mg.).

The results of the experiment are summarized in Table 3.

It will be observed in this experiment that with one exception the controls all died before the 90th day, whereas only 2 of 10 treated animals died during this period. Among the remaining 8 animals, 5 showed an increase in weight in contrast with the regular decrease in controls. The lesions in the treated animals contrast markedly with those in the untreated animals.

It occurred to us at this point in our work that the results we had produced might be due to taurin alone, instead of taurin in combination with the other substances, and the next experiment (Experiment 4) was designed to test what result in treatment could be produced with taurin alone. Unfortunately, the dose employed in this experiment was the same as had been employed in Experiment 2, and when administered intraperitoneally it led to death so rapidly in the controls that the curative effect of the taurin alone or in combination was not as evident as in the last experiment.

EXPERIMENT 4

The same emulsion of tubercle bacilli suspended in sterile salt solution which had been employed in the second experiment and which had been kept in the icebox about 2 weeks, on April 2, 1914, was inoculated into 16 guinea-pigs and in the same dose, that is to say, approximately $\frac{1}{38}$ of a culture, but instead of subcutaneously as in the earlier experiment, they were inoculated directly in the peritoneal cavity. They were then subdivided into 2 groups of 8 each, 1 of which was kept untreated as a control. The 2nd group were treated for the most part with taurin alone, but a few of the animals toward the end were given from 2 to 4 doses of the gold-chlorid sodium-oleate combination in addition. The average weight of these animals was 450 gm. As the treatment differed somewhat, they had best be considered separately. The results of the experiment are expressed in Table 4.

In this experiment the control animals died more rapidly than in previous experiments, owing to the large intraperitoneal injections,

TABLE 4

RESULTS OF EXPERIMENT 4

Guinea-Pig	No. of Injections	Time of Treatment	Day of Death	Weight (gm.) — = Loss + = Gain		Postmortem Examination
7	.....	.....	41st	—120		Guinea-pigs 7, 3, 1, and 2 all showed diffuse tuberculous peritonitis with tubercles covering peritoneum and omentum, diffuse nodes of the lung, liver and spleen enlarged, with small tubercles
3			45th	— 95		
1			47th	—130	Av.	
2	Controls		47th	—105	loss	
11			48th	— 55	106	Guinea-pigs 11, 5, 4, and 6 showed conditions in the organs essentially similar to those described in the first group, except that in 5 and 11 peritonitis was not marked. Lymph nodes enlarged and caseated in all 8 animals
5			50th	—145	gm.	
4			56th	— 80		
6			56th	—115		
10	11 (.12—.15 gm. (taurin)	1 mo.	52nd	—120		Guinea-pigs 10, 16, 9, 8, 15, and 13 all showed a moderate number of tubercles in lung, liver, and spleen, but few on peritoneum and omentum. Lymphatic glands caseated only in Nos. 10 and 15, in the glands of which small central areas were softened
16	14 (taurin).....	.....	57th	+ 30		
9	11 (.12—.15 gm. (taurin)	1 mo.	61st	— 40		
8	15 (taurin).....	7 wk.	61st	—130		
15	16 (taurin).....	7 wk.	62nd	—110		
13	16 (taurin and 2 combination treatments)	.....	64th	—135	Av. loss 19 gm.	
14	16 (taurin and 4 combination treatments)	.....	Killed on 88th	+210		Guinea-pigs 12 and 14 showed no tubercles in lung, liver, spleen, or peritoneum. Lymph glands enlarged and hardened
12	16 (taurin and 4 combination treatments)	.....	Killed on 88th	+140		

and all showed diffuse lesions, including tuberculous peritonitis. The controls had all died before the treated animals, with one exception (treated animal No. 10). All the controls showed a marked loss of weight, whereas 3 of the treated animals actually gained in weight, in spite of the death of one of them (16). The appearance of the treated animals post mortem also differed distinctly from that of the untreated animals. Two animals (12 and 14) appeared to have been cured of the more rapid infection.

In the subsequent experiments to be reported at this time rabbits instead of guinea-pigs were used, and they were infected with bovine tubercle bacilli.

EXPERIMENT 5

Six rabbits, averaging in weight about 2000 gm., were given intravenous injections of 10 mg. each of a culture of Bacillus tuberculosis bovinus, designated G, grown 6 months on glycerin broth (isolated

TABLE 5

RESULTS OF EXPERIMENT 5

Rabbit	No. of Injections	Day of Death	Weight (gm.) — = Loss + = Gain		Postmortem Examination
			CONTROLS		
684		44th	−450		Lungs filled with diffuse masses of tubercles which microscopically showed necrotic areas and lymphoid, epithelioid, and giant cells in considerable numbers. Liver appeared normal in gross,, but in microscopic section showed small well-localized tubercles containing epithelioid and lymphoid cells with some central necrosis in places. Spleen appeared normal both in gross and on microscopic examination. Lymph nodes enlarged and caseated
659	Controls	63rd	−450	Av. loss 383 gm.	Lung full of diffuse tubercles. Practically no crepitation. Microscopically, it showed many diffuse necrotic areas with lymphoid, epithelioid, and giant cells. Spleen was enlarged and congested, and showed a few areas of epithelioid and lymphoid cells, without distinct caseation. Liver apparently normal. Microscopically, it was congested, but without tubercles. Kidney showed a few discrete tubercles near cortex, containing epithelioid and lymphoid cells. Lymph glands enlarged with areas of caseation
633		71st	−250		Liver apparently normal in the gross, but on section it contained small areas of lymphoid and epithelioid cells. Kidney contained small tubercles with many epithelioid and a few lymphoid cells. Peritoneal cavity contained 50 c.c. of exudate and many tubercles. Lung filled with large masses of caseated diffuse tubercles with large necrotic areas and lymphoid, epithelioid, and many giant cells. Tubercle bacilli could be stained in the necrotic areas. Spleen enlarged; no tuberculosis
645	31 (taurin).	Killed on 44th	+400		Liver normal. Lung showed a few very discrete areas containing large epithelioid and plasma cells surrounded by lymphoid cells. No tubercle bacilli found in these areas. Spleen and mesenteric lymph nodes apparently normal
601	40 (taurin).	78th	+100	Av. gain 400 gm.	Lung revealed a very few well-localized nodes similar to those of the last animal. Lower left lobe showed gangrene. Liver apparently normal in the gross. On section numerous tubercles found, with areas of necrosis containing epithelioid, lymphoid, and giant cells. Coccidiosis. Some of the areas of necrosis surrounded by young connective-tissue cells. Kidney normal. Spleen and lymph nodes apparently normal
672	43 (taurin).	Killed on 78th	+700		Lung contained numerous well-circumscribed nodules with slight areas of caseation. No tubercle bacilli found. Some of these areas invaded by fairly dense and recent connective tissue. Kidney normal. Liver congested, but normal

from tuberculous glands in 1911 by Dr. Paul Lewis, of Philadelphia). Three days after inoculation the treatment of 3 animals (601, 645, and 672) was begun; they were given from 31 to 43 doses of 0.5 gm. each of taurin dissolved in 7.5 c.c. of distilled water, every day, over a period of about 7 weeks. The result of this experiment is briefly outlined in Table 5.

In this experiment only one of the treated animals died, whereas all the controls died. The one treated animal which died (601) contained coccidiosis, and the evidence of tuberculosis was not marked. The lesions in the lungs showed very striking contrasts in the control animal that died on the 44th day, as compared with the one killed at that period (684 and 645). It was impossible, however, to demonstrate tubercle bacilli in the lesions of the two treated animals (601 and 645), and only a very few were seen in the third treated animal (672), whereas they were evident in numbers in the untreated controls. Altho the experiment contains few animals, it gives distinct evidence of the arrest and beginning of repair of the tubercles.

EXPERIMENT 6

In the final experiment, 20 rabbits, averaging about 1600 gm. in weight, were given intraperitoneal injections of 1 mg. of the same culture used in the last experiment, bovine bacillus G, from the surface of a glycerin broth culture aged 11 weeks, and were divided into 4 series, one of which was left as a control.

In the 2nd series treatment was begun 3 days after inoculation, in the 3rd series 7 days after, and in the 4th series 14 days after. The 2nd series was given 28 injections of 0.5 gm. of taurin intravenously on alternate days, and the 3rd and 4th series 28 injections of the same dosage and frequency. The number of doses was somewhat less in the few animals that died during the course of the experiment. The results of this experiment are tabulated in Table 6.

In this experiment, then, it is evident that the rabbits were in nearly every instance completely cured of an infection which was fatal to the controls in all but a single instance (786). This last animal showed advanced lesions of the lungs, tho it had survived to 143 days and had actually gained in weight.

SUMMARY AND CONCLUSIONS

This report deals with the curative effect of taurin alone or in combination with a colloidal mixture of sodium gold chlorid and

TABLE 6

RESULTS OF EXPERIMENT 6

Rabbit	Day of Death	Weight (gm.) −− = Loss. + = Gain		Postmortem Examination
		SERIES 1. CONTROLS		
773	19th	−750		Small tubercles of the lung and peritoneum. Retroperitoneal lymph glands enlarged. Spleen and liver normal
782	50th	−100		Rabbits 782 and 787—similar lesions. Lung contained many diffuse tubercles, and necrotic areas with giant and lymphoid cells and numerous tubercle bacilli. Liver—no marked change. Spleen enlarged without visible tubercles. Peritoneum rough with small tubercles. Lymph nodes enlarged and caseated
787	50th	−400	Av. loss 200 gm.	
780	141st	− 50		Lung contained many diffuse tubercles with caseation. Lymph nodes enlarged and caseated. Peritoneum roughened. Spleen and liver showed no tubercles
786	Killed on 143rd	+300		Similar to Rabbit 780
		SERIES 2. TREATED ANIMALS		
772	50th	−800		Peritoneum was rough and contained 30 c.c. clear exudate. Retroperitoneal lymph glands somewhat enlarged. All other organs apparently normal
769	Killed on 156th	+500	Av. gain 220 gm.	Rabbits 769, 815, and 816 showed an absolutely normal appearance, with the exception of slightly enlarged lymph nodes. No foci of tuberculosis found microscopically
815		+500		
816		+450		
790		+450		Lung contained a few well-localized tubercles, which showed thickened alveolus septa, and a small focus infiltrated with lymphoid cells. No tubercle bacilli found in lesion
		SERIES 3		
783	99th	−800		Lung showed a small focus of pneumonia, but no definite nodules. Liver showed two areas of coccidiosis. Kidney and spleen congested; no tubercles
771	Killed on 156th	+200	Av. gain 40 gm.	No lesions visible in these animals
777		+200		
773		+150		
774		+450		
		SERIES 4		
776	99th	−250		Showed a pneumonic area in one lung. Organs otherwise normal
784	Killed on 156th	+150	Av. gain 60 gm.	These animals showed no lesions. Retroperitoneal lymph glands somewhat enlarged, but not caseated
759		+200		
781		+100		
W		+100		

sodium oleate in experimental tuberculosis in guinea-pigs and rabbits. Apparently as favorable results were obtained with taurin alone as with taurin combined with sodium gold chlorid and sodium oleate. From preliminary tests taurin may be injected in as large and probably in much larger doses than were employed, either subcutaneously or intravenously, without any symptomatic disturbance.

Guinea-pigs were infected with either bovine or human strains of tubercle bacilli. The results were similar with both. In nearly every instance the controls all died before any of the treated animals, and whereas the controls lost weight almost uniformly, the treated animals gained. The majority of the treated animals were killed for observation many days after the controls had all died. The contrast in the extent of visible tuberculosis between controls and treated animals was marked. Whereas the process was advanced in the controls, it was arrested and in some instances apparently cured in the treated animals. The success of the treatment varied naturally in accordance with the variations in infecting dose, the route of inoculation, and the time of beginning treatment, as specified in the protocols. In all experiments and in nearly every instance the results were distinct, and in many instances startling. The process of the disease was arrested and apparently cured when treatment was begun as late as 3 weeks after infection.

Rabbits were infected with intraperitoneal or intravenous injections of bovine tubercle bacilli and treatment was carried out by intravenous injections of taurin alone. The results were similar, but even more marked than in guinea-pigs. Otherwise fatal infections, which in evolution were slower than in guinea-pigs, were not only arrested, but evidence of them often definitely disappeared. Histologic examinations of organs in these experiments showed in treated animals arrested tubercles, absence of caseation, disappearance of tubercle bacilli in the lesions, and evidence of repair by connective-tissue ingrowth, as controlled by the advancing lesions, with caseation and numerous bacilli in the controls. A number of treated animals showed minimal evidences of tuberculosis, and in no inconsiderable number the tissues were essentially normal microscopically. In such successful cases treatment was begun as late as 2 weeks after inoculation.